Public health impact of switching from a 4-valent to a 9-valent HPV vaccination programme in Chile

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Introduction

- In Chile, a school-based vaccination program with the human papillomavirus quadrivalent vaccine (4vHPV; HPV6/11/16/18) was introduced into the National Immunisation Programme (NIP)
  - For 9-year-old girls in 2014[1]
  - For 9-year-old boys in 2019[1]
- High and sustained vaccination coverage rate since the HPV programme introduction (~80%)[2]

Objective

- To estimate the expected public health impact of a gender-neutral vaccination (GNV) programme with a nonavalent HPV vaccine (9vHPV HPV6/11/16/18/31/33/45/52/58) compared to the current programme with 4vHPV

Methods

- A previously developed dynamic transmission mathematical model (**Figure 1**)[3-5] was adapted to evaluate the impact of switching from a 4vHPV to 9vHPV programme for 9-year-old girls and boys in Chile for the prevention of HPV-related cervical cancer; cervical lesions (CIN-1/2/3); vaginal, vulvar, penile, anal, and head and neck cancers; as well as genital warts (GW) and recurrent respiratory papillomatosis (RRP), over a 100-year time horizon
- The model projected 80% coverage for the current strategy (4vHPV) and alternative scenario (9vHPV)
- Chile-specific data were used from literature where available; default values were used otherwise. Input data included demographic, behavioral and epidemiological and screening parameters (**Table 1**)
- The model assumed a two-dose schedule, lifelong immunity following vaccination, herd immunity and ongoing cytology screening
- The outcomes were incidence reduction and incremental averted cases and deaths of cervical cancer (CC), cervical intraepithelial neoplasia (CIN) 1-3 and non-cervical cancers (vagina/vulva/anus/head and neck/penis) with 9vHVP compared to 4vHPV

Figure 1. Simplified schematic diagram of the initial compartments for HPV infection and disease progression

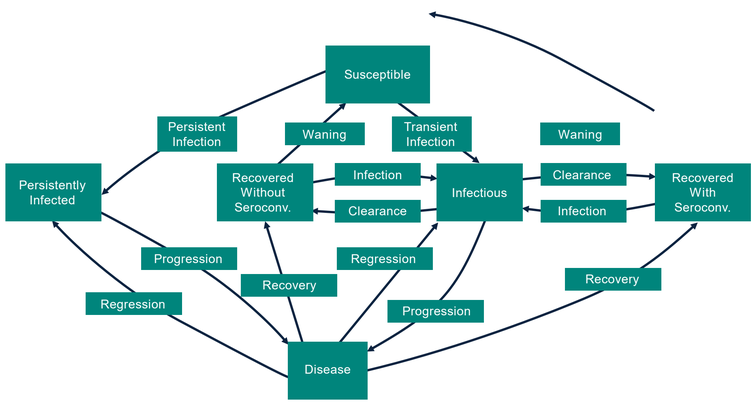


Table 1. Potential burden of HPV-related diseases in Chile and HPV attribution fraction

	Burden of disease			Relative contribution		
	Incidence[a] per 100,000	Mortality[a] per 100,00	HPV AF (%)	6/11 (%)	16/18 (%)	16/18/31/33/45/52/58 (%)
Female						
Genital warts[6,b]	430	–	100	90	–	
RRP[7,c]	1.12	0.05	100	90	–	
Cervical[8,9]	15.5	8.20	100	–	68.2	87.2
Vaginal[8,9]	0.51	0.20	78	–	46.6	59.7
Vulvar[8,9]	1.3	0.64	40.1	–	28.1	34
Anal[8,9]	0.88	0.21	90.4	–	72.6	83.4
Oral cavity[8,9]	1.30	0.56	22	–	84.9	89.7
Oropharynx[8,9]	0.54	0.20	31	–	84.9	89.7
Larynx[8,9]	0.28	0.18	24	–	84.9	89.7
Male						
Genital warts[6,b]	430	–	100	90	–	–
RRP[7,c]	1.12	0.05	100	90	–	–
Penile[8,9]	0.99	0.43	51	–	72.6	83.4
Anal[8,9]	0.52	0.12	90.4	–	84.9	89.7
Oral cavity[8,9]	1.80	0.81	22	–	84.9	89.7
Oropharynx[8,9]	0.71	0.42	31	–	84.9	89.7
Larynx[8,9]	2.00	1.30	24	–	84.9	89.7

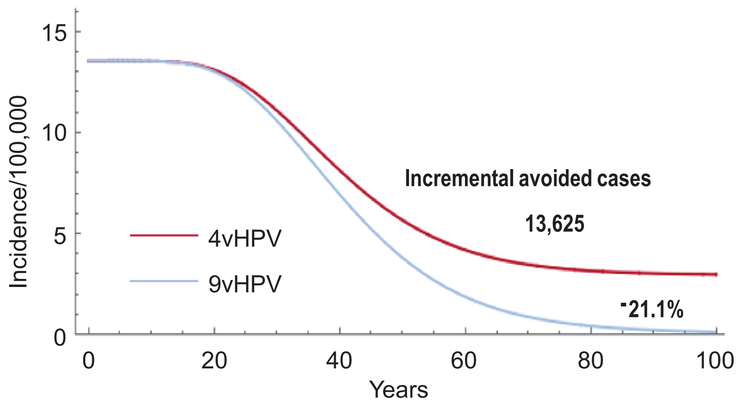
[a]Crude rate per 100,000 inhabitants.
[b]Based on Latin America literature data; [c]Based on international literature data.
AF, attribution fraction; HPV, human papillomavirus; RRP, recurrent respiratory papillomatosis.

Results

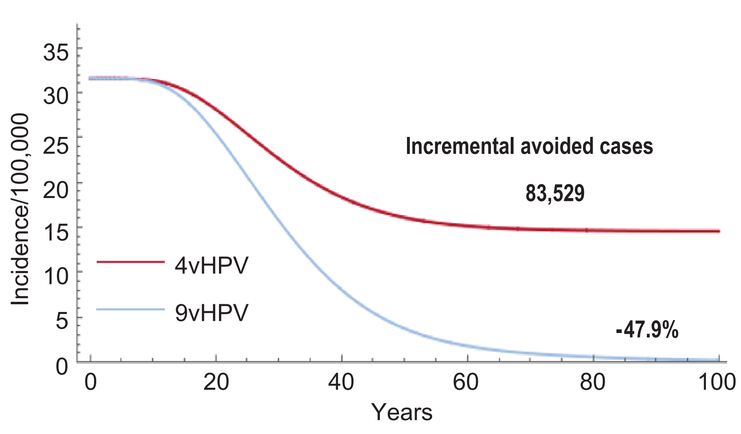
- Compared to the current vaccination programme, after 100 years, a 9vHPV GNV programme was estimated to further reduce:
  - The incidence of female HPV diseases: cervical cancer by 21.1%; CIN2/3 by 47.9%; CIN1 by 56.2%; anal cancer by 11.3%; head and neck cancer by 2.6% (**Figures 2A, 2B; Table 2**)
  - The incidence of male HPV diseases: penile cancer by 5.8%; anal cancer by 6%; and head and neck cancer by 3.6% (**Figures 2C**, **2D**; **Table 2**)
  - 143,353 cases (142,999 female cancers/CIN 1-3 and 354 male cancers) and 7,388 deaths (**Tables 2, 3**)

Figure 2. Projection of reduction of HPV-related diseases using 4vHPV and 9vHPV over 100 years. A. Cervical cancer; B. CIN 2/3; C. Head and neck cancer (males); D. Penile cancer

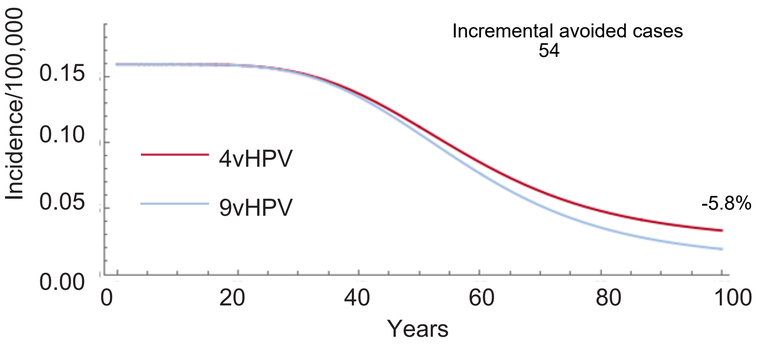
2A. Cervical cancer



2B. CIN 2/3



2C. Penile cancer (males)



2D. Head and neck (males)

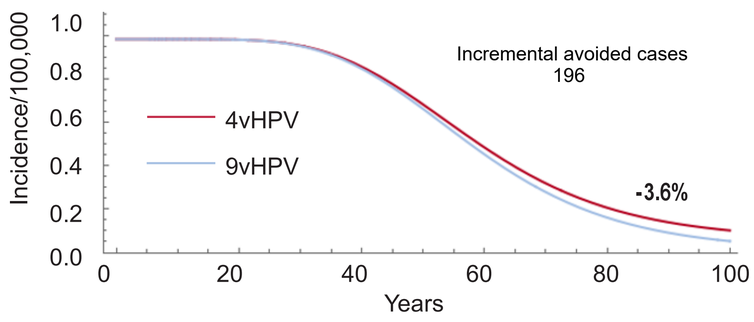


Table 2. Incidence reduction and additional avoided cases with 9vHPV relative to 4vHPV over 50 and 100 years

HPV-related disease	Incidence	Frequency	Incidence	Frequency
	Over 50 years		Over 100 years	
Cervical cancer	4.8	2,340	21.1	13,625
CIN 1	28.0	12,868	56.2	45,012
CIN 2/3	21	22,937	47.9	83,529
Vaginal cancer	1.0	4	8.3	51
Vulvar cancer	3.2	32	22.2	334
Anal cancer (female)	1.8	48	11.3	389
Anal cancer (male)	1.0	14	6.0	104
Head/neck cancer (female)	0.4	7	2.6	59
Head/neck cancer (male)	0.5	18	3.6	196
Penile cancer	0.7	5	5.8	54
Total		38,273		143,353

Table 3. Additional avoided deaths with 9vHPV relative to 4vHPV over 50 and 100 years

HPV-related disease	Incidence	Frequency	Incidence	Frequency
	Over 50 years		Over 100 years	
Cervical cancer	3.8	1,008	19.4	6,938
Vaginal cancer	0.8	1	7.8	19
Vulvar cancer	2.7	11	21.1	131
Anal cancer (female)	1.6	13	10.7	114
Anal cancer (male)	0.8	4	5.6	33
Head/neck cancer (female)	0.3	2	2.3	25
Head/neck cancer (male)	0.4	8	3.4	105
Penile cancer	0.6	2	5..5	23
Total		1,049		7,388

Limitations

- Model assumes a high and sustained vaccination coverage rate over 100 years
- Model does not assess possible changes to cervical cancer screening methods over the course of the 100 years

Conclusions

- In Chile, switching from 4vHPV to 9vHPV is projected to provide:
  - A substantial public health impact in terms of reduction of HPV-related disease and death in both genders
  - Faster and greater reduction in the incidence of cervical cancer/precursors and non-cervical cancers due to additional protection against HPV 31/33/45/52/58 relative to the current strategy

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